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**From:** Rick Reiss [rreiss@exponent.com]  
**Sent:** 10/23/2020 3:40:15 PM  
**To:** Lowit, Anna [Lowit.Anna@epa.gov]; Perron, Monique [Perron.Monique@epa.gov]  
**Subject:** New paper on OP inhibition  
**Attachments:** Kasteel2020\_Article\_AcetylcholinesteraseInhibition (1).pdf

Anna and Monique,

Prior to our meeting next week, I wanted to make you aware of a new paper out of Europe that may be relevant to our discussion. The authors are from regulatory authorities including EFSA. They had a similar idea as we did in evaluating interspecies and intraspecies differences in inhibition.

Some key points in the paper include:

1. They used IC50 values instead of the bimolecular rate constant. This is consistent with the SAP recommendation in that it directly uses the in vitro concentrations. The IC50 is calculated with in vitro inhibition measurements at a single time point. While I do not necessarily agree that this is the best way, we will show some calculations using the IC50 which results in lower variability.
2. They include three OPs, including chlorpyrifos, diazinon and phosmet (their oxons specifically) and two carbamates.
3. They used electric eel and human blood sources. Electric eel AChE is known to be more reactive than human AChE (which the study confirms) so it is not very useful for interspecies analysis. They concede in the discussion that using rat AChE would have been a better choice.
4. They have 20 human blood donors and estimate variability in the human population with these data (we had a similar sample size of 18). They recommend that the default intraspecies UF can be reduced to 1.4 (diazinon) to 2.2 (chlorpyrifos).

Rick

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